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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,645	10/31/2000	Rainer Haas	100564-00035	6963

6449 7590 02/10/2005

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/673,645	Applicant(s) HAAS ET AL.	
	Examiner Carla Myers	Art Unit 1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 January 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on *21 January 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *53,57,58,60-63 and 65-103*.
   Claim(s) withdrawn from consideration: *59*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Carla Myers
CARLA J. MYERS
PRIMARY EXAMINER

Continuation of 3. NOTE: The amendment to the claims to recite that the probes are specific for nucleic acid sequences which encompass a region corresponding to one or more nucleotides selected from nucleotides 2032, 2057, 2057, 2059, 2503 and 2611 raises new issues under 35 U.S.C. 112 second paragraph. The specification does not provide a clear definition for what is intended to be encompassed by nucleotides which correspond to one another and there is no fixed definition for this term in the art as it applies to nucleic acids.For example, it is not clear as to whether 'corresponding' sequences are identical to one another, or are complementary to one another or share some unstated degree of complementarity or identity. It is thereby unclear as to whether, for example, corresponding nucleotides are identical nucleotides at identical positions or whether corresponding nucleotides may be different nucleotides at different locations that are within some unstated proximity to the reference nucleotide position .

Continuation of 11. does NOT place the application in condition for allowance because: for the reasons of record in view of the non-entry of the after final amendment. Further, if the amendments were entered, Applicants arguments are not directed to limitations recited in the claims. In the response, Applicants cite Vester as teaching that mutations at positions 2032, 2057, 2058, 2059, 2611 are associated with macrolide resistance in a number of microorganisms. However, the non-entered claims are not limited to methods in which the presence of a specific mutation at position 2032, 2057, 2058, 2059 or 2611 is detected as indicative of macrolide antibiotic resistance. Rather, the claims broadly recite a method in which a probe is hybridized to a nucleic acid that encompasses a region corresponding to the positions 2032, 2057, 2058, 2059 and 2611. The claims do not require the detection of a mutation at the stated positions, but rather require only the hybridization of a probe to a nucleic acid that encompasses this region. There are no process steps which specifically require the detection of a specific mutation - the claims only require detecting hybridization between a probe and a sample nucleic and thereby allow for the hybridization of the probe to wildtype sequences. Also, in view of the 'corresponding' language, the claims are not limited to probes which hybridize to nucleic acids containing the recited nucleotide position, but rather include probes which hybridize to nucleic acids which include other nucleotide positions. Further, this post-filing date reference highlights the unpredictability in the art in teaching that 'it might be expected that the higher the level of phylogenetic conservation of a base the more drastic would be the phenotypic consequence of changing it. Surprisingly, this is not always the case" (see page 6). Veseter (Table 4) teaches that "It is expected that macrolide resistance conferred by rRNA mutations is more likely to arise in the bacteria in the upper portion of the table." The reference does not teach that in the bacteria set forth in the lower portion of the table or in the bacteria not listed in the table, macrolide antibiotic resistance can be evaluated by detecting a mutation at 2032, 2057, 2058, 2059 or 2611. It is also noted that Vester does not address the issue as to the prevalence of the 2503 mutation in microorganisms and its association with macrolide resistance. With respect to the 103 rejection, Applicants argue that the six positions recited in the claims are not listed in the table of Amann as being within a region of the rRNA that is accessible for probe hybridization. However, as discussed above, the claims are not limited to probes which hybridize to only a region of rRNA that includes nucleotide positions 2032, 2057, 2058, 2059, or 2611. Also, the claims do not include any length limitation for the probes such that the probes would hybridize only to the sequences taught by Amann as being accessible for hybridization. Additionally, claims 86-90 are drawn to kits and there is no requirement that the probes in the kit be useful for hybridization in situ and thereby no requirement that the probes fall within the region of rRNA that Amann teaches as being accessible for in situ hybridization. The recitation in claims 86-90 of the intended use of the kit - i.e., "for determining macrolide antibiotic resistance in microorganisms by in situ hybridization" - does not distinguish the claimed kits over the the kits suggested by the prior art for use in general hybridization methods to detect macrolide resistance. Applicants further traverse the rejection by arguing that "one skilled in the art could not have predicted that a set of oligonucleotides could be found which would be able to discriminate among point mutations in rRNA of microorganisms under identical conditions." However, Applicants are arguing limitations not recited in the claims. The claims do not require the use of a particular set of probes, do not require the simultaneous use of a particular set of probes, and do not require discriminating among point mutations using probes. It is noted that the proposed amendment would, however, overcome the rejection of the claims under 35 U.S. C. 112, second paragraph.